REMARKS

By the foregoing amendments, claims 13 and 14 have been amended. Support for the amendments to claims 13 and 14 can be found in the specification in the paragraph spanning pages 5-6; Examples 1 and 3; and original claim 14.

Information Disclosure Statement

The Information Disclosure Statement submitted on September 3, 2008, is objected to because several references are listed without translations for consideration. Applicants respectfully point out that the Information Disclosure Statement of September 3, 2008, states on page 1 that, in accordance with 37 CFR § 1.98(a)(3)(i), the relevance of EP 0309324; EP 1400531; EP 1403278 and DE 197 21 290, is set forth in their abstracts, the English translations of which are attached to the references. Further, the relevance of the remaining non-English references was set forth in the corresponding patents and applications listed in table on page 1 of the Information Disclosure Statement, all of which were provided in the Information Disclosure Statement and considered by the Examiner.

Applicants believe they have fully complied with the provisions of 37 CFR § 1.98(a)(3), and that the non-English references should therefore be considered of record. Reconsideration is respectfully requested.

The Rejection under 35 USC § 103(a)

Claims 13-14 are rejected under Section 103(a) as unpatentable over Guez et al., WO 99/25374 or US 6,653,336, in view of Eyjolfsson, WO 03/059388, and www.signetchem.com.

Guez et al. teaches the combination of perindopril, indapamide and microcrystalline cellulose. The Signet sheets teach microcrystalline cellulose with low moisture content. Guez et al. do not teach the use of a molar ratio of 1 to 0.1-0.9 or of 1 to 0.50-0.83 for perindopril to inorganic carbonate. Eyjolfsson teaches inclusion of carbonates in ACE inhibitor formulations. Eyjolfsson teaches a preferred ratio of perindopril to carbonate less than 1:1. Nonetheless, the Examiner maintains that it would have been obvious to the skilled artisan to optimize a perindopril to carbonate ratio to the non-preferred ratio of Eyjolfsson, i.e., a perindopril to carbonate molar ratio greater than 1:1, and combine it with the teachings of Guez et al. to produce the subject invention.

Although Applicants do not agree, they have in the interest of expediting prosecution, removed the prior limitation relating to molar ratio of perindopril and carbonate, and have instead amended claim 13 to recite that the "components of said pharmaceutical composition have low moisture content or are substantially anhydrous, whereby said pharmaceutical composition has 0.07 wt% or less diketopiperazine (DKP) content after three weeks storage at 50ºC in a closed container."

Eyjolfsson uses water in his granulation process and his pharmaceutical compositions do not have components that are low moisture content or substantially anhydrous. There is no suggestion in Guez et al. or Eyjolfsson that anhydrous or low moisture components be used, whereby the pharmaceutical composition has 0.07 wt% or less DKP content after three weeks storage at 50°C in a closed container. Applicants note that Eyjolfsson analyzes in Example 3, page 5, the stability of quinapril tablets of Examples 1 and 2, at 40ºC for 9 days; they were found to produce a diketopiperazine content of 0.2 and 0.3%, respectively. This data, which Applicants note is for quinapril, a different but related ACE inhibitor, indicates a more rapid degradation to DKP in tablets produced according to Eyjolfsson as compared to the subject composition. It is further noted that the test according to Eyjolfsson was shorter and conducted at a lower temperature (40ºC, 9 days), yet produced more DKP than the test (50ºC, 21 days) according to the subject invention, clearly indicating that Eyjolfsson does not suggest the composition of claim 13.

While www.signetchem.com may offer the possibility of low moisture microcellulose, it does not specifically suggest a pharmaceutical composition having a 0.07 wt% or less DKP content after three weeks storage at 50ºC in a closed container. For these reasons, it is submitted that claims 13 and 14 are not *prima facie* obvious.

Applicants also note that Eyjolffson contains the specific negative proviso (page 3, lines 15-16) that the formulation does not contain a substantial amount of a saccharide compound. Guez et al. describe compositions in Examples 1 and 2 that comprise an ACE inhibitor, a diuretic, and the saccharides, lactose and microcrystalline cellulose. In view of the specific teaching away in Eyjolffson from saccharides, the skilled artisan would not have been motivated to combine the saccharides of Guez et al. with the carbonate of Eyjolffson. Therefore, it is additionally submitted on the basis that the prior art teaches away from the combination of the relevant elements, that *prima facie* obviousness has not been established.

Claims 15-17 are rejected under Section 103(a) over Guez et al. in view of Eyjolfsson as applied to claims 13 and 14 above, in view of www.signetchem.com, and further in view of Cooper et al., U.S. Pat. Publication 2003/0232796.

www.signetchem.com teaches the availability in 2002 of microcrystalline celluloses with different properties, sizes and forms. Cooper et al. teach the use of nanoparticles of active agents including diuretics but does not specifically mention indapamide.

Applicants respectfully point out that neither www.signetchem.com nor Cooper et al. supply the deficiencies of Guez et al. and Eyjolfsson, because neither of these references teach or suggest the recitation in claim 13 that the "components of said pharmaceutical composition have low moisture content or are substantially anhydrous, whereby said pharmaceutical composition has 0.07 wt% or less diketopiperazine (DKP) content after three weeks storage at 50°C in a closed container." It is therefore submitted that claim 13 and dependent claims 15-17 are non-obvious over the combination of Guez et al., Eyjolfsson, www.signetchem.com and Cooper et al. Withdrawal of the subject rejection is respectfully requested.

Closing Remarks

For the reasons set forth above, Applicants respectfully submit that the claims are allowable over the art of record and reconsideration and issuance of a notice of allowance are respectfully requested. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

It is believed that no new claim fees are required. Submitted herewith are a Request for Continued Examination and a Petition for Extension of Time for one month (large entity). It is believed that no other fees are due with this submission. If any additional fees are required, please charge such fees to Deposit Account No. 19-5117.

Respectfully submitted,

Dated: June 3, 2009

/Margaret M. Wall/

Margaret M. Wall, #33,462
Swanson & Bratschun, L.L.C.
8210 SouthPark Terrace
Littleton, Colorado 80120
Telephone: 303.268.0066
Facsimile: 303.268.0065

S:\ClientFolders\0183 (Uexkull & Stolberg)\09\OA Response 2009-06-03.doc